

June 2, 2015

**Phase I/II Opdivo (nivolumab) Trial Shows Bristol-Myers Squibb's
PD-1 Immune Checkpoint Inhibitor is First to Demonstrate Anti-Tumor Activity
In Patients With Hepatocellular Carcinoma**

(PRINCETON, NJ, May 29, 2015) – Bristol-Myers Squibb Company (NYSE: BMY) announced results from an interim analysis of CA209-040, a Phase I/II dose-ranging trial evaluating the safety and anti-tumor activity of Opdivo (nivolumab) in previously-treated patients with hepatocellular carcinoma (HCC) or advanced liver cancer. Initial findings demonstrated that the estimated survival rate in evaluable patients (n=47) was 62% at 12 months. Results also show the safety profile of Opdivo is generally consistent with that previously-reported for Opdivo in other tumor types.

Through the collaboration agreement entered into in September 2011 between ONO and BMS, ONO granted BMS exclusive rights to develop and commercialize Opdivo in the rest of the world, except in Japan, Korea and Taiwan where ONO had retained all rights to develop and commercialize the compound. In July 2014, ONO and BMS signed a new collaboration agreement in which the companies agreed to jointly develop and commercialize Opdivo, ipilimumab and three early-stage immunotherapies in Japan, South Korea and Taiwan.

In USA, Opdivo was approved under accelerated approval for the treatment of unresectable or metastatic melanoma and disease progression following Yervoy and, if BRAF V600 mutation positive, a BRAF inhibitor in December 2014 and approved for the treatment of metastatic squamous NSCLC with progression on or after platinum-based chemotherapy in March 2015. Also, BMS has a robust clinical development program in a variety of tumor types overseas, including: Renal Cell Carcinoma (RCC), Head and Neck Cancer, Blood Cancer, Glioblastoma, Colorectal Cancer, Pancreatic Cancer, Gastric Cancer, Hepatocellular Carcinoma, Triple-Negative Breast Cancer, Small-Cell Lung Cancer, Bladder Cancer. In Japan, ONO launched it for the treatment of unresectable melanoma in September 2014. Also, ONO is conducting clinical development programs including RCC, NSCLC, Head and Neck Cancer, Gastric Cancer, Esophageal Cancer, Hepatocellular Carcinoma and Hodgkin Lymphoma.

Attached from the following page is the press release made by BMS for your information.

Contact

ONO PHARMACEUTICAL CO., LTD.

Corporate Communications

public_relations@ono.co.jp



Phase I/II *Opdivo* (nivolumab) Trial Shows Bristol-Myers Squibb's PD-1 Immune Checkpoint Inhibitor is First to Demonstrate Anti-Tumor Activity In Patients With Hepatocellular Carcinoma

- *Interim results show favorable safety profile of Opdivo, and durable responses in previously-treated patients*
- *Overall survival rate of 62% at 12 months observed at this interim analysis*
- *Hepatocellular carcinoma is the second most frequent cause of cancer-related death worldwide and remains an area of significant unmet medical need*
- *Patients with hepatocellular carcinoma who have relapsed or have disease progression, following standard of care, have a median survival with best supportive care of ~7 to 8 months*

(PRINCETON, NJ, May 29, 2015) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) today announced results from an interim analysis of CA209-040, a Phase I/II dose-ranging trial evaluating the safety and anti-tumor activity of *Opdivo* (nivolumab) in previously-treated patients with hepatocellular carcinoma (HCC) or advanced liver cancer. Initial findings demonstrated that the estimated survival rate in evaluable patients (n=47) was 62% at 12 months. Results also show the safety profile of *Opdivo* is generally consistent with that previously-reported for *Opdivo* in other tumor types. These data will be featured today, May 29, during the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) press briefing at 1:00 – 2:00 p.m. CDT and presented on Saturday, May 30 from 8:27 a.m. – 8:39 a.m. CDT (Late Breaking Abstract #101).

“Hepatocellular carcinoma is an aggressive and fatal cancer, comprising 90 percent of all liver cancer in adults worldwide with limited therapeutic options for patients with advanced stage disease; no treatment advances have been made for patients who fail to respond or progress on the current standard of care,” said Anthony B. El-Khoueiry, MD, lead study author and associate professor of clinical medicine and phase I program director at the University of Southern California Norris Comprehensive Cancer Center. “These preliminary data are encouraging and support the ongoing evaluation of nivolumab in this patient population, as they show promising preliminary survival data, and durable partial or complete response in one out of five nivolumab-treated patients, with many others experiencing stable disease.”

More than 700,000 people around the world are diagnosed with HCC each year with a majority of all HCC cases caused by infection with the hepatitis B virus (HBV) or hepatitis C virus (HCV),

making HBV/HCV the most common risk factor for liver cancer worldwide. Patients with advanced HCC receiving the current standard of care have a median overall survival of less than 1 year. For patients who have relapsed or have disease progression, median survival with best supportive care is approximately 7 to 8 months.

“Bristol-Myers Squibb’s experience in hepatitis and Immuno-Oncology make us poised as leaders to advance *Opdivo* into additional studies of hepatocellular carcinoma,” said Michael Giordano, senior vice president, Head of Development, Oncology, Bristol-Myers Squibb. “*Opdivo* has demonstrated improvements in survival in a number of different tumor types. We are excited that this trial has shown the potential that this may extend to advanced liver cancer and hope to confirm these findings in future trials.”

About the CA209-040

CA209-040 is a Phase I/II dose-ranging trial that evaluated the safety and anti-tumor activity of *Opdivo* in patients with HCC, the majority of whom had received prior treatment. The trial included 47 HCC patients who were enrolled into one of three treatment arms depending on whether or not they were infected with HCV or HBV. Patients enrolled in the trial received *Opdivo* doses ranging from 0.1 – 10 mg/kg intravenously every 2 weeks for up to 2 years. The primary objective was safety, tolerability, dose limiting toxicities, and maximum tolerated dose. Anti-tumor activity was a secondary objective (using RECIST 1.1 criteria), and overall survival was an exploratory objective.

As of this interim analysis, 62% of patients in the study were still alive after 12 months. Eight (19%) patients (of 42 evaluable patients) achieved a complete or partial response, meaning that the size of their tumors measured at baseline decreased by 30–100% with *Opdivo* treatment. In patients with response, duration of response ranged from more than 1.4 – 12.5 months. Seventeen patients remained on study treatment and 30 discontinued treatment due to progressive disease (n=26), complete response (n=2), or adverse events (n=2).

CA209-040 is the first trial to characterize the safety profile of *Opdivo* monotherapy in patients with HCC, including those with HCV and HBV infections. In the trial, safety and tolerability were well-characterized, with the frequency and intensity of treatment-related adverse events (AEs) being consistent across *Opdivo* dose levels. The majority of side effects were mild to moderate in nature with abnormal liver enzymes (19% AST and 15% ALT), rash (17%) and elevation of amylase (15%) and lipase (17%) being the most common; the abnormal liver enzymes and elevated amylase and lipase were not accompanied by any significant clinical symptoms. Grade 3–4 treatment-related AEs were infrequent (19%). There were no treatment-related deaths reported.

About Opdivo

Bristol-Myers Squibb has a broad, global development program to study *Opdivo* in multiple tumor types consisting of more than 50 trials – as monotherapy or in combination with other therapies – in which more than 8,000 patients have been enrolled worldwide.

Opdivo became the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world on July 4, 2014 when Ono Pharmaceutical Co. announced that it received manufacturing and marketing approval in Japan for the treatment of patients with unresectable melanoma. In the U.S., the U.S. Food and Drug Administration (FDA) granted its first approval for *Opdivo* for the treatment of patients with unresectable or metastatic melanoma and disease progression following *Yervoy* (ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor. On March 4, 2015, *Opdivo* received its second FDA approval for the treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy.

IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

- Severe pneumonitis or interstitial lung disease, including fatal cases, occurred with OPDIVO treatment. Across the clinical trial experience in 691 patients with solid tumors, fatal immune-mediated pneumonitis occurred in 0.7% (5/691) of patients receiving OPDIVO; no cases occurred in Trial 1 or Trial 3. In Trial 1, pneumonitis, including interstitial lung disease, occurred in 3.4% (9/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Immune-mediated pneumonitis occurred in 2.2% (6/268) of patients receiving OPDIVO; one with Grade 3 and five with Grade 2. In Trial 3, immune-mediated pneumonitis occurred in 6% (7/117) of patients receiving OPDIVO, including, five Grade 3 and two Grade 2 cases. Monitor patients for signs and symptoms of pneumonitis. Administer corticosteroids for Grade 2 or greater pneumonitis. Permanently discontinue OPDIVO for Grade 3 or 4 and withhold OPDIVO until resolution for Grade 2.

Immune-Mediated Colitis

- In Trial 1, diarrhea or colitis occurred in 21% (57/268) of patients receiving OPDIVO and 18% (18/102) of patients receiving chemotherapy. Immune-mediated colitis occurred in 2.2% (6/268) of patients receiving OPDIVO; five with Grade 3 and one with Grade 2. In Trial 3, diarrhea occurred in 21% (24/117) of patients receiving OPDIVO. Grade 3 immune-mediated colitis

occurred in 0.9% (1/117) of patients. Monitor patients for immune-mediated colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO for Grade 2 or 3. Permanently discontinue OPDIVO for Grade 4 colitis or recurrent colitis upon restarting OPDIVO.

Immune-Mediated Hepatitis

- In Trial 1, there was an increased incidence of liver test abnormalities in the OPDIVO-treated group as compared to the chemotherapy-treated group, with increases in AST (28% vs 12%), alkaline phosphatase (22% vs 13%), ALT (16% vs 5%), and total bilirubin (9% vs 0). Immune-mediated hepatitis occurred in 1.1% (3/268) of patients receiving OPDIVO; two with Grade 3 and one with Grade 2. In Trial 3, the incidences of increased liver test values were AST (16%), alkaline phosphatase (14%), ALT (12%), and total bilirubin (2.7%). Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater transaminase elevations. Withhold OPDIVO for Grade 2 and permanently discontinue OPDIVO for Grade 3 or 4 immune-mediated hepatitis.

Immune-Mediated Nephritis and Renal Dysfunction

- In Trial 1, there was an increased incidence of elevated creatinine in the OPDIVO-treated group as compared to the chemotherapy-treated group (13% vs 9%). Grade 2 or 3 immune-mediated nephritis or renal dysfunction occurred in 0.7% (2/268) of patients. In Trial 3, the incidence of elevated creatinine was 22%. Immune-mediated renal dysfunction (Grade 2) occurred in 0.9% (1/117) of patients. Monitor patients for elevated serum creatinine prior to and periodically during treatment. For Grade 2 or 3 serum creatinine elevation, withhold OPDIVO and administer corticosteroids; if worsening or no improvement occurs, permanently discontinue OPDIVO. Administer corticosteroids for Grade 4 serum creatinine elevation and permanently discontinue OPDIVO.

Immune-Mediated Hypothyroidism and Hyperthyroidism

- In Trial 1, Grade 1 or 2 hypothyroidism occurred in 8% (21/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Grade 1 or 2 hyperthyroidism occurred in 3% (8/268) of patients receiving OPDIVO and 1% (1/102) of patients receiving chemotherapy. In Trial 3, hypothyroidism occurred in 4.3% (5/117) of patients receiving OPDIVO. Hyperthyroidism occurred in 1.7% (2/117) of patients, including one Grade 2 case. Monitor

thyroid function prior to and periodically during treatment. Administer hormone replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism.

Other Immune-Mediated Adverse Reactions

- In Trial 1 and 3 (n=385), the following clinically significant immune-mediated adverse reactions occurred in <2% of OPDIVO-treated patients: adrenal insufficiency, uveitis, pancreatitis, facial and abducens nerve paresis, demyelination, autoimmune neuropathy, motor dysfunction, and vasculitis. Across clinical trials of OPDIVO administered at doses 3 mg/kg and 10 mg/kg, additional clinically significant, immune-mediated adverse reactions were identified: hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barré syndrome, and myasthenic syndrome. Based on the severity of adverse reaction, withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone- replacement therapy.

Embryofetal Toxicity

- Based on its mechanism of action, OPDIVO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO and for at least 5 months after the last dose of OPDIVO.

Lactation

- It is not known whether OPDIVO is present in human milk. Because many drugs, including antibodies, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from OPDIVO, advise women to discontinue breastfeeding during treatment.

Serious Adverse Reactions

- In Trial 1, serious adverse reactions occurred in 41% of patients receiving OPDIVO. Grade 3 and 4 adverse reactions occurred in 42% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse drug reactions reported in 2% to <5% of patients receiving OPDIVO were abdominal pain, hyponatremia, increased aspartate aminotransferase, and increased lipase.
- In Trial 3, serious adverse reactions occurred in 59% of patients receiving OPDIVO. The most frequent serious adverse drug reactions reported in $\geq 2\%$ of patients were dyspnea, pneumonia, chronic obstructive pulmonary disease exacerbation, pneumonitis, hypercalcemia, pleural effusion, hemoptysis, and pain.

Common Adverse Reactions

- The most common adverse reactions ($\geq 20\%$) reported with OPDIVO in Trial 1 were rash (21%) and in Trial 3 were fatigue (50%), dyspnea (38%), musculoskeletal pain (36%), decreased appetite (35%), cough (32%), nausea (29%), and constipation (24%).

Please see [U.S. Full Prescribing Information](#) for OPDIVO.

Immuno-Oncology at Bristol-Myers Squibb

Surgery, radiation, cytotoxic or targeted therapies have represented the mainstay of cancer treatment over the last several decades, but long-term survival and a positive quality of life have remained elusive for many patients with advanced disease.

To address this unmet medical need, Bristol-Myers Squibb is leading research in an innovative field of cancer research and treatment known as Immuno-Oncology, which involves agents whose primary mechanism is to work directly with the body's immune system to fight cancer. The company is exploring a variety of compounds and immunotherapeutic approaches for patients with different types of cancer, including researching the potential of combining Immuno-Oncology agents that target different pathways in the treatment of cancer.

Bristol-Myers Squibb is committed to advancing the science of Immuno-Oncology, with the goal of changing survival expectations and the way patients live with cancer.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit www.bms.com or follow us on Twitter at <http://twitter.com/bmsnews>.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee Opdivo will receive regulatory approval for an additional indication in hepatocellular carcinoma or advanced liver cancer.

Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2014 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

###

Contacts:

Media: Carrie Fernandez, 215-859-2605, carrie.fernandez@bms.com

Priyanka Shah, 908-447-6134, priyanka.shah1@bms.com

Investors: Ranya Dajani, 609-252-5330, ranya.dajani@bms.com

Bill Szablewski, 609-252-5864, william.szablewski@bms.com